

# Physical Activity Patterns and Exercise Performance in Cardiac Transplant Recipients

Jonathan Myers, PhD; Lars Gullestad, MD; Daniel Bellin, MS; Heather Ross, MD; Randall Vagelos, MD; Michael Fowler, MD

- **BACKGROUND:** Cardiac transplantation (CTX) improves exercise tolerance, but CTX recipients still achieve only 50% to 70% of normal values for exercise capacity. Among the factors suggested to explain the reduced exercise tolerance in CTX recipients is deconditioning. Little is known about the relation between physical activity patterns and exercise test responses in CTX patients.
- **METHODS:** Forty-seven CTX patients (mean age 47 ± 12 years; mean 4.8 ± 3.0 years after CTX) underwent maximal exercise testing and assessment of current and past physical activity patterns using a questionnaire. Energy expenditure from recreational and occupational activities over the last year and for adulthood were expressed in kcal/week and correlated with peak oxygen consumption (VO<sub>2</sub>), VO<sub>2</sub> at the ventilatory threshold, and the percentage of age-predicted peak VO<sub>2</sub> achieved.
- RESULTS: The patients reported expending a mean of approximately 1100 kcal/week in recreational activity, suggesting a moderate level of physical activity is maintained after CTX. The mean peak VO<sub>2</sub> achieved for the group was 17.2 ± 5.2 mL/kg/min, corresponding to 59% ±14% of age-predicted exercise capacity. Significant but modest associations were observed between recreational energy expenditure during the last year and percentage of age-predicted peak VO<sub>2</sub> achieved (r = 0.34, P < .01), and VO<sub>2</sub> at the ventilatory threshold (r = 0.45, P < .01). Energy expenditure from blocks walked and stairs climbed per week was modestly associated with peak VO<sub>2</sub> (r = 0.36, P < .05), percentage of predicted peak VO<sub>2</sub> achieved (r = 0.39, P < .01), and VO<sub>2</sub> at the ventilatory threshold (r = 0.42, P < .01). Exercise capacity was poorly related to occupational and recreational activities when expressed as average weekly energy expended throughout adulthood.
- **CONCLUSION:** Post-CTX patients maintain a moderately active lifestyle. Measures of exercise tolerance generally are related to recent daily recreational activities in CTX patients, but these associations are modest. The many physiologic factors unique to CTX recipients likely play a more important role than deconditioning in determining exercise tolerance in these patients.

### KEY WORDS

exercise testing transplantation energy expenditure

From the Cardiovascular Division,
Veterans Affairs Palo Alto Health Care
System; and Stanford University
School of Medicine, Palo Alto, Calif.
Address correspondence to:
Jonathan Myers, PhD, Cardiology, 111C, VA Health Care System, 3801
Miranda Avenue, Palo Alto, CA 94304
(e-mail: drj993@aol.com).

Over the last three decades, cardiac transplantation (CTX) has become a successful and widely accepted treatment for patients with end-stage chronic heart failure, and this procedure improves exercise tolerance.<sup>1,2</sup> However, for reasons that are not completely understood, CTX only partially restores exercise capacity to normal; transplant

recipients achieve only about 50% to 70% of values predicted for age and gender.<sup>1,3,4</sup> Although the factors that have been suggested to explain persistent exercise intolerance in CTX recipients include immunosuppressive therapy, a low chronotropic reserve associated with denervation, decreased skeletal muscle strength, decreased

capillary density, and characteristics associated with rejection, <sup>2,4-9</sup> one of the most important may be deconditioning associated with physical inactivity. <sup>9-12</sup> In part for this reason, regular physical activity is now widely recommended for CTX patients. Favorable effects of exercise rehabilitation in these patients include improvements in peak oxygen consumption (VO<sub>2</sub>), reduced blood lactate concentration, reduced perceived effort for the same work demands, improved submaximal endurance, lessened symptoms of dyspnea and fatigue, and increased muscle strength and lean body mass. <sup>10-13</sup>

Habitual physical activity is an important determinant of exercise capacity among healthy individuals. 14,15 In CTX patients, physical activity patterns may be limited by comorbidities, fear on the part of the patient, or concerns by the treating physician about limitations imposed by CTX. Information on the relationship between habitual activity and peak VO2 may provide insight into the extent to which deconditioning contributes to reduced exercise tolerance in CTX patients. At present, little is known about physical activity patterns among CTX recipients. The purpose of the current study was to: 1) describe daily occupational and recreational physical activity patterns in CTX recipients, and 2) determine the association between physical activity patterns and exercise test performance in these patients. We hypothesized that an association would exist between physical activity patterns and exercise performance in this population.

#### **METHODS**

### **Patients**

Forty-seven patients (41 male, 6 female; mean age 47  $\pm$  12 years) participated in the study. All were post-orthotopic cardiac transplant, and the mean duration between transplantation and exercise testing was 4.8  $\pm$  3.0 years. Clinical characteristics of the study group are presented in Table 1.

#### **Exercise Testing**

Symptom-limited maximal exercise tests were performed in the upright position using an electrically braked cycle ergometer at a constant cadence of 60 rpm. A continuous ramp protocol was used in which the work rate was increased by 10 W/min. Ventilatory oxygen uptake was measured using a Medical Graphics Corporation 2001 system (St. Paul, Minn). Gas exchange data were obtained breath-by-breath and recorded every 30 seconds. Ventilatory oxygen uptake, carbon dioxide production, minute ventilation, and respiratory exchange ratio were calculated on-line. The percentage of age-predicted normal peak VO<sub>2</sub> was

**Table 1 •** BASELINE CLINICAL CHARACTERISTICS OF THE STUDY POPULATION (N = 47)

|                                    | Mean ± SD          |
|------------------------------------|--------------------|
| Age, y                             | 46.7 ± 11.6        |
| Gender, M/F                        | 41 (87%) / 6 (13%) |
| Height, cm                         | 175.8 ± 9.7        |
| Weight, kg                         | 83.5 ± 17.9        |
| Body mass index, kg/m <sup>2</sup> | $30.0 \pm 5.4$     |
| Peak VO <sub>2</sub> , mL/kg/min   | 17.2 + 5.2         |
| Medications                        | No. (%)            |
| Calcium antagonist                 | 22 (47)            |
| • Diuretics                        | 4 (9)              |
| ACE-inhibitor                      | 14 (30)            |
| Hydralazine                        | 2 (4)              |
| Alpha-blocker                      | 4 (9)              |
| Beta-blocker                       | 4 (9)              |

VO<sub>2</sub>, oxygen consumption; ACE, angiotensin-converting enzyme.

determined for each patient using the equation of Wasserman et al. <sup>16</sup> The ventilatory threshold was determined by two experienced independent reviewers using the V-slope method <sup>17</sup> and confirmed by ventilatory criteria. Heart rate was recorded continuously by electrocardiography and blood pressure was recorded every 2 minutes throughout the test using a semi-automated recorder (Quinton STBP-68, Quinton Instruments, Seattle, Wash). Chronotropic reserve was quantified as (peak heart rate–resting heart rate/age-predicted maximal heart rate–resting heart rate).

### **Physical Activity Questionnaire**

The quantification of physical activity was performed by questionnaire and modeled after the Harvard Alumni studies of Paffenbarger and colleagues.<sup>18</sup>

An abridged version of the questionnaire is presented in Appendix 1. The questionnaire was self-administered during a clinic visit, but subjects were encouraged to ask questions if necessary to clarify their responses. The questionnaire responses were entered into a Microsoft ACCESS File, which computed metabolic costs of both occupational and recreational activities, and expressed the results as energy expenditure in kcal/week. Energy costs of activities were estimated from the compendium of physical activities developed by Ainsworth et al.19 Energy cost of stairs climbed per week was calculated using the estimation of Basset et al.20 For reference, one flight of stairs climbed was considered 10 steps, and 12 blocks was considered 1 mile. Energy expenditure was expressed in terms of both lifetime adulthood recreational and occupational, and separately as energy expended during the year prior to undergoing exercise testing. Because few of the subjects were working at the

time of evaluation, occupational energy expenditure was not quantified for the past year.

#### **Statistics**

Data are expressed as mean ± SD. The association between estimations of energy expenditure and exercise test performance measures was determined using standard linear correlations.

### **RESULTS**

The major reason given for terminating exercise was fatigue or leg fatigue in 46 patients; dyspnea was the major reason for stopping in only 1 patient. Exercise test responses of the subjects are presented in Table 2. Noteworthy responses included a mean resting heart rate of  $94 \pm 12$  beats/min (supine), and  $100 \pm 25$  beats/min (sitting), a peak heart rate of  $129 \pm 18$  beats/min ( $74\% \pm 14\%$  of age-predicted), chronotropic reserve was 0.40, peak watts achieved was  $104 \pm 37$ , and peak VO<sub>2</sub> was  $17.2 \pm 5.2$  mL/kg/min, representing  $59\% \pm 14\%$  of the age-predicted maximum. Oxygen uptake at the ventilatory threshold occurred at a mean of 55% of peak VO<sub>2</sub>.

Combining current blocks walked and stairs climbed, a mean of  $514 \pm 448$  kcal were expended per week. As a reference, 500 kcal corresponds to roughly 60 blocks walked, 250 flights of stairs climbed, or a combination

#### Table 2 • EXERCISE TEST RESULTS

|                                   | Mean ± SD        |
|-----------------------------------|------------------|
| Rest                              |                  |
| Heart rate (supine), beats/min    | $94 \pm 12$      |
| Heart rate (sitting), beats/min   | $100 \pm 25$     |
| Systolic blood pressure (mm Hg)   | $145 \pm 16$     |
| Diastolic blood pressure (mm Hg)  | 88 + 12          |
| Ventilatory threshold             |                  |
| VO <sub>2</sub> (L/min)           | $0.765 \pm 0.19$ |
| VO <sub>2</sub> (mL/kg/min)       | $9.4 \pm 2.6$    |
| VE (L/min)                        | $24.1 \pm 6.0$   |
| VCO <sub>2</sub> (L/min)          | $0.680 \pm 0.18$ |
| Respiratory exchange ratio        | $0.89 \pm 0.06$  |
| Maximal exercise                  |                  |
| Heart rate                        | $129 \pm 18$     |
| Exercise time, min                | $9.4 \pm 3.6$    |
| VO <sub>2</sub> (L/min)           | $1.40 \pm 0.42$  |
| VO <sub>2</sub> (mL/kg/min)       | 17.2 + 5.2       |
| Percent predicted VO <sub>2</sub> | $59 \pm 14$      |
| VE (L/min)                        | $62.1 \pm 18$    |
| VCO <sub>2</sub> (L/min)          | $1.650 \pm 0.52$ |
| Respiratory exchange ratio        | $1.18 \pm 0.09$  |
| Watts                             | 104 + 37         |
| Systolic blood pressure           | $178 \pm 29$     |
| Diastolic blood pressure          | 83 ± 17          |

 $\mathrm{VO}_{2}$ , oxygen consumption; VE, minute ventilation;  $\mathrm{VCO}_{2}$ , carbon dioxide production.

of these per week.  $^{19,20}$  For recreational activities, subjects expended a mean of  $1631 \pm 2314$  kcal/week during adulthood, and a mean of  $1154 \pm 1241$  kcal/week over the last year. A mean of  $9141 \pm 4546$  kcal/week were expended during adulthood occupational activities. Twenty subjects (42%) reported that they expended  $\leq 500$  kcal/week in recreational activities, 7 (15%) reported expending > 500 to  $\leq 1000$  kcal/week, 5 (11%) reported expending > 1000 to 1500 kcal/week, 5 (11%) reported expending  $\geq 1500$  to 2000 kcal/week, and 10 (21%) reported expending  $\geq 2000$  kcal/week.

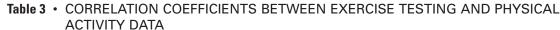
Correlation coefficients between occupational and recreational energy expenditure and exercise test responses are presented in Table 3. Peak VO2 was significantly related only to energy expended by blocks walked and stairs climbed (r = 0.36, P < .05). Peak VO<sub>2</sub> was poorly related to recreational activities during adulthood and over the last year. The percentage of agepredicted peak VO2 achieved was modestly related to  $VO_2$  at the ventilatory threshold (r = 0.53, P < .01), energy expended by blocks walked and stairs climbed (r = 0.39, P < .01), and recreational activities during the last year (r = 0.34, P < .05). Energy expended from recreational activities performed over the last year also was related to  $VO_2$  at the ventilatory threshold (r = 0.45, P < .01), and to energy expenditure by blocks walked/stairs climbed (r = 0.48, P < .01). Energy expended by both occupational and recreational activities throughout adulthood was poorly related to measures of exercise capacity.

#### **DISCUSSION**

In the current study, we sought to describe activity patterns in post-CTX recipients and to determine the association between these activity patterns and exercise test performance. We observed that CTX recipients engage in moderate levels of activity and the average energy expenditure was only modestly associated with exercise capacity.

#### **Exercise Test Responses in CTX Patients**

Denervation of the donor heart as a result of transplantation markedly alters the normal cardiovascular homeostasis, which has a considerable influence on the response to exercise. These alterations include absence of normal afferent and efferent nervous control, impairment of the renin-angiotensin system leading to altered vasoregulatory control and central hemodynamics, and elimination of the subjective sensation of angina. Exercise tolerance values observed in the current study were typical of CTX patients in that our patients achieved only 59% of the peak VO<sub>2</sub> values predicted for age and gender. Other noteworthy responses included a heightened resting heart rate (100 beats/min sitting), a peak heart rate of only 129 beats/min



|   |                                      | % Predicted<br>VO <sub>2</sub><br>achieved | VO <sub>2</sub> at<br>ventilatory<br>threshold | Blocks<br>walked<br>and flights<br>climbed | Energy Expenditure |           |              |  |
|---|--------------------------------------|--|--|--|--------------------|-----------|--------------|--|
|   | Peak<br>VO <sub>2</sub><br>mL/kg/min |  |  |  | Recreational       |           | Occupational |  |
|   |                                      |  |  |  | Last<br>year       | Adulthood | Adulthood    |  |
| Peak VO <sub>2</sub> mL/kg/min<br>% Predicted VO <sub>2</sub> | 1                                    |  |  |  |                    |           |              |  |
| achieved  | 0.60*                                | 1  |  |  |                    |           |              |  |
| VO <sub>2</sub> at ventilatory                                |                                      |  |  |  |                    |           |              |  |
| threshold   | 0.83*                                | 0.53*                                      | 1  |  |                    |           |              |  |
| Blocks walked and   |                                      |  |  |  |                    |           |              |  |
| flights climbed   | 0.36†                                | 0.39*                                      | 0.42*  | 1  |                    |           |              |  |
| Energy expenditure  |                                      |  |  |  |                    |           |              |  |
| Recreational  |                                      |  |  |  |                    |           |              |  |
| Last year   | 0.04                                 | 0.34*                                      | 0.45*  | 0.48*                                      | 1                  |           |              |  |
| Adulthood   | 0.13                                 | -0.17                                      | -0.12  | -0.05                                      | 0.04               | 1         |              |  |
| Occupational  |                                      |  |  |  |                    |           |              |  |
| Adulthood   | -0.03                                | -0.16                                      | 0.18   | -0.07                                      | -0.26              | 0.17      | 1            |  |

VO<sub>2</sub>, oxygen consumption.

(74% of predicted), and the ventilatory threshold occurred at a level corresponding to only approximately 2.5 METs. Similar to previous studies, the chronotropic reserve was reduced (0.40).9 Thus, despite the well-documented benefits of CTX on survival and quality of life,<sup>21</sup> exercise capacity remains markedly reduced relative to individuals with intact hearts of similar age.

### **Physical Activity Patterns in CTX Patients**

Our patients reported recreational energy expenditure values of roughly 1100 kcal/week over the year prior to undergoing exercise testing. Although energy expenditure has varied widely in the many studies performed among apparently healthy individuals, these values suggest that post-CTX patients engage in activities in the low to moderate range of energy expenditure. 18,19 This suggests that CTX does not overtly limit activity levels per se. Naturally, specific activities and volume of energy expended will depend upon overall health, comorbid conditions, and duration of time since CTX. Interestingly, recent recreational activity (post-CTX) was reported to be roughly the same as that expended throughout adulthood. These observations are consistent with previous data suggesting that more than half of post-CTX patients return to work or engage in pre-CTX daily activities.<sup>22</sup>

# **Association Between Physical Activity and Exercise Test Performance**

In addition to the physiologic factors mentioned above, deconditioning is frequently suggested as a fac-

tor contributing to exercise intolerance in CTX patients. Among the activity patterns we measured, peak VO<sub>2</sub> was significantly related only to current energy expenditure expressed as blocks walked and flights of stairs climbed per week. Peak VO2 was poorly associated with both recent and remote occupational and recreational activity. VO<sub>2</sub> at the ventilatory threshold was significantly related to energy expenditure from blocks walked and stairs climbed and recent recreational activities, but these associations were modest (r = 0.42 and 0.45, respectively; P< .01). It is interesting to note that energy expenditure expressed as blocks walked and stairs climbed had the strongest association with measures of exercise capacity. This is likely due to the fact that energy expenditure expressed in these terms is more readily quantifiable than the widely varying leisure time activities. In addition, walking and stair climbing are activities that all ambulatory individuals perform to one extent or another during the day.

There are several potential explanations why physical activity patterns do not more closely reflect treadmill performance in CTX recipients. The patients' condition clearly limits the range of activities that they are capable of performing. The relatively narrow range of values for both recreational activities and peak VO<sub>2</sub> contributes to the two being poorly correlated. The possibility that our questionnaire did not accurately reflect physical activity patterns also must be considered. The limitations of quantifying energy expenditure by questionnaire have been characterized by a number of investigators.<sup>23,24</sup> Although the Harvard

<sup>\*</sup>P < .01.

<sup>†</sup>P < .05.

Alumni Questionnaire is well recognized and has provided strong support for the association between activity status and cardiovascular morbidity and mortality, <sup>18</sup> whether it adequately reflects activity patterns in post-transplant patients has not been studied. In addition, we have not validated the questionnaire using any of the various activity recording devices. There have been numerous approaches to assessing physical activity patterns, including accelerometers, pedometers, heart rate recording devices, and observational techniques, <sup>24</sup> in addition to the many questionnaire approaches. Differences in the approach to quantifying energy expenditure may explain at least some of the differences in the results of studies associating physical activity and exercise capacity.

The relatively modest associations between activity status and exercise test performance we observed suggest that factors other than physical activity patterns play a more important role in determining exercise tolerance in CTX recipients. These factors include physiologic characteristics unique to CTX, such as immunosuppressive therapy, a low chronotropic reserve limiting cardiac output (heart rate increased only 28 beats/min in the current study), and skeletal muscle factors such as decreased capillary density and reduced muscle strength.4-9 We were interested strictly in the association between physical activity patterns and exercise tolerance in this population, but it should be noted that the determination of peak VO2 is complex. Many multivariate models to predict peak VO2 have been developed among normal subjects and patients with cardiovascular disease, and factors such as age, gender, smoking history, and body mass index in addition to physical activity patterns have been shown to contribute to the variance in peak VO<sub>2</sub> 4,9,14,25

#### **Previous Studies**

The current results concur with previous studies in which associations between exercise capacity and physical activity patterns generally are lower among those with cardiovascular disease compared to healthy individuals. It should be noted that while our study was designed to assess general (lifetime and recent) activity status, most studies have addressed activity levels acutely (eg. activity sensors over a 1-day period). However, we are not aware of any other studies specifically addressing the relation between activity patterns and exercise capacity in posttransplant recipients, although three studies have addressed this issue in patients with chronic heart failure. Mezzani and colleagues<sup>26</sup> reported that habitual activity level, expressed as a score, was significantly related to peak VO<sub>2</sub> in both healthy subjects and patients with heart failure. However, the relationship was weak in the patients with chronic heart failure (r = 0.48). Using

limb movement sensors, Davies et al<sup>27</sup> and Oka et al<sup>28</sup> reported relatively poor associations between daily activity levels and peak VO2 in patients with chronic heart failure. Among apparently healthy subjects, results of studies assessing the relationship between physical activity patterns and peak VO2 have been mixed. Berthouze et al<sup>25</sup> reported a strong association (r = 0.92) between peak  $VO_2$  and mean daily energy expenditure (using a questionnaire) among healthy men and women between 18 and 88 years of age. The above mentioned study of Mezzani et al<sup>26</sup> similarly found a strong correlation (r = 0.83) between peak VO<sub>2</sub> and activity level using their score in a subgroup of healthy subjects. Conversely, Leon et al,29 using the Minnesota Leisure Time Activity Questionnaire, reported correlation coefficients of only 0.41 and 0.44 between total and heavy leisure time physical activity, respectively, and treadmill time in healthy middleaged men. Skinner and coworkers<sup>30</sup> reported correlations of only 0.13 and 0.21, respectively, between total daily and occupational energy expenditure and exercise performance in a group of apparently healthy adults.

## Limitations

In addition to the transplant-related factors mentioned above, metabolic factors in the peripheral musculature and strength strongly influence exercise capacity after CTX<sup>13</sup>; we did not have metabolic or strength measures among our subjects. As mentioned, many physiologic factors influence exercise tolerance after CTX. An investigation into all of the physiologic determinants of peak VO<sub>2</sub> in CTX patients was not the purpose of our study, and most of these measurements were not available in our sample. As with any questionnaire approach, the responses depend on patient recollection and how judicious they may be in their responses. The questionnaire used, although validated in other populations, has not been used previously among CTX recipients. Our subjects represented a consecutive group referred for exercise testing, and they varied widely in terms of age, time since CTX, and energy expenditure. A more homogenous sample may have provided different results; therefore, our findings may not be generalizable to all CTX recipients.

#### Summary

A mean of 5 years after CTX, patients exhibit activity levels in the low to moderate range of energy expenditure. Exercise test performance is only modestly associated with physical activity patterns. This suggests that physiologic factors unique to CTX, rather than deconditioning, play a more important role in explaining exercise intolerance in these patients.

## Appendix I • ABRIDGED PHYSICAL ACTIVITY QUESTIONNAIRE

In conjunction with your treadmill test today, we are asking you some questions regarding your current and past patterns of physical activity. It is very important that you be as specific as possible when filling out this questionnaire, so please do not hesitate to ask questions if any part of it is unclear.

|           | nysical Activities Within the Last Year  How many city blocks or their equivalent do you walk on a typi  blocks walked per day   | cal day? (1 mile walked i                           | is about 12 blocks  | )                       |  |  |  |
|-----------|--|---|---|-------------------------|--|--|--|
| 2.        | What is your usual pace of walking? (check one)  ☐ Casual or strolling (less than 2 mph)  ☐ Fairly brisk (3 to 4 mph)  | ☐ Steady, light pace (2<br>☐ Brisk or striding (4 m | ·   |                         |  |  |  |
| 3.        | . How many flights of stairs do you climb each day? (10 steps are about 1 flight) flights/day  |   |   |                         |  |  |  |
| 4.        | List all sports or recreational activities you have actively particips sports or events, such as skiing or swimming. Record the num you participated in the activity in the designated spaces.  Bicycling times/year  Carpentry (outside house) times/year  Lawn and garden times/year  (Followed by extensive list of activities)                         | ber of times/year and the avg # hrs avg # hrs       |   |                         |  |  |  |
| Pl<br>lis | nysical Activities in Adulthood ease check the occupations listed below you have held as an added below apply to you, use the "other" option at the end of the Occupational Activities  Heavy or major cleaning (eg, wash car, wash windows, mop Serving food-standing and walking  Plumbing or Electrician  Other   | e list to state your occupa                         | ,   | none of the occupations |  |  |  |
|           | (Followed by extensive list of activities)   |   |   |                         |  |  |  |
| 2.        | Recreational Activities In your adult life, what recreational activities have you regularly below and be as specific as possible. Please give careful consi   Generally, I have not participated in recreational activities on  Bicycling  Walking leisurely (2 to 3 mph)  Walking briskly (3 to 4 mph)  Other  (Followed by extensive list of activities) | deration to the "other" o                           | ategory at the enderse avg # hrs<br>avg # hrs<br>avg # hrs<br>avg # hrs | d.<br>yrs<br>yrs<br>yrs |  |  |  |

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